Mathematical Models of Tumour Angiogenesis and Simulations(Theory of Bio-Mathematics and Its Applications)

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Mathematical Models of Tumour Angiogenesis and Simulations

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Abstract: We study parabolic-ODE systems proposed by Othmer and Stevens [11] and Anderson and Chaplain [1],[2] respectively. According to Levine and Sleeman [10], we reduce them to corresponding evolution equations and show the existence of time global solutions by the method of energy respectively. Then we discuss a mathematical relationship between these models and find a common property to them. Finally we show some results of numerical experiments of a mathematical model proposed by Othmer amd Stevens, which are carried out by the conservative upwind finite difference approximation proposed by Saito and Suzuki [12].

1 Introduction

We begin with a brief explanation about tumour angiogensis.

1.Tumour produces TAFs(some chemicals) as a trigger of tumour angiogenesis. They diffuse and reach neighboring capillaries and other blood vessels.
2. In response to TAFs EC(endothelial cells) surface begins to develop pseudopodia which penetrate the weakened basement membrane.
3. Capillary sprouts continue to grow in length out of the parent vessels and form loops leading to microcirculation of blood.
4. The resulting capillary network continues to progress and eventually invades the tumour colony.

The above sequent procedure is called *tumour angiogenesis*, which permits the tumour to grow further.

In [11] H.G. Othmer and A. Stevens derived a parabolic-ODE system modelling chemotactic aggregation of myxobacteria, where unknown functions $P = P(x,t)$ and $W = W(x,t)$ stand for the density of the bacteria and that of control species, respectively. That is,

$$P_t = D\nabla \cdot [P\nabla(\log(P/\Phi(W)))] \tag{1.1}$$

$$W_t = F(W,P) \qquad \text{in} \quad \Omega \times (0,\infty) \tag{1.2}$$

with flux-zero condition

$$P\nabla(\log(P/\Phi(W))) \cdot \nu = 0 \qquad \text{on } \partial\Omega \times (0,T) \tag{1.3}$$

and

$$P(x,0) = P_0(x) \geq 0, \qquad W(x,0) = W_0(x) > 0, \quad \text{in} \quad \Omega, \tag{1.4}$$

where Ω is a bounded domain in $\boldsymbol{R}^n$ with smooth boundary $\partial\Omega$, $D > 0$ is a constant and ν denotes the outer unit normal vector. In fact, [11] provides the reinforced random walk on lattice points as in Davis [3], takes the renormalized limit, and gets the above system. By the numerical computation [11] classified the solution according to its behaviour as $t \to +\infty$:

1.(aggregation) $\liminf_{t\to\infty} \|P(\cdot,t)\|_{L^\infty} > \|P(\cdot,0)\|_{L^\infty}$ and $\|P(\cdot,t)\|_{L^\infty} < C$ for all t.
2.(blowup)$\|P(\cdot,t)\|_{L^\infty}$ becomes unbounded in finite time.
3.(collapse)$\limsup_{t\to\infty} \|P(\cdot,t)\|_{L^\infty} < \|P(\cdot,0)\|_{L^\infty}$.

This method of mathematical modelling has gained the understanding of tumour angiogenesis in Levine and Sleeman [10] by giving the sensitivity function

$$\Phi(W) = (\frac{W+\alpha}{W+\beta})^a \tag{1.5}$$

for the prescribed constants α,$\beta > 0$ and a. Throughout this paper we call (1.1)-(1.4) with (1.5) *Othmer-Stevens model with linear growth* and *exponential growth* when $F(P,W) = P + W$ and PW respectively.

In this paper, we first review Othmer-Stevens model with exponential growth(cf.[7]-[9]). Next we prove the existence of time global solution to (1.1)-(1.4) with (1.5) for $a > 0$ and $F(P, W) = -WP$, which is called *Othmer-Stevens model with uptake* in this paper. In the same way, we show the existence of time global solution to a prabolic ODEs system modelling tumour angiogenesis by Anderson and Chaplain, which is called *Anderson-Chaplain model* thoughout this paper(cf. [9]). We further discuss a mathematical relationship between these models and a common property to them. Finally we proceed the numerical experiments concerning simplified Othmer-Stevens model with linear growth in the case of $n = 1$ and observe that there are decaying traveling waves.

2 Othmer-Stevens model

2.1. Exponential growth case for $a < 0$

In this subsection we consider the problem (1.1)-(1.4) for $a < 0$ and $F(W, P)= WP$. Mathematical analysis of this model was done by Levine and Sleeman [10]. In fact, taking $\log W = \Psi$, we get $\Psi_t = P$ because of $W_t/W = P$ and it holds

$$\Psi_{tt} = D\Delta\Psi_t - \nabla\cdot\left(\frac{aD(\beta-\alpha)e^{\Psi}}{(e^{\Psi}+\alpha)(e^{\Psi}+\beta)}\Psi_t\nabla\Psi\right) \quad \text{in} \quad \Omega\times(0,T) \tag{2.1}$$

from (1.1) and (1.2). Then our problem is reduced to the the following:

$$(TM)\begin{cases} P[\Psi] = \Psi_{tt} - D\Delta\Psi_t + \nabla\cdot\left(\frac{aD(\beta-\alpha)e^{\Psi}}{(e^{\Psi}+\alpha)(e^{\Psi}+\beta)}\Psi_t\nabla\Psi\right) = 0 & \text{in} \quad \Omega\times(0,T) \\ \frac{\partial}{\partial\nu}\Psi|_{\partial\Omega} = 0 & \text{on } \partial\Omega\times(0,T) \\ \Psi_t(x,0) = P_0(x), \quad \Psi(x,0) = \log W_0(x) & \text{in} \quad \Omega. \end{cases}$$

In [10], Levine and Sleeman replaced the coefficient

$$\frac{a(\beta-\alpha)e^{\Psi}}{(e^{\Psi}+\alpha)(e^{\Psi}+\beta)} = \frac{a(\beta-\alpha)W}{(W+\alpha)(W+\beta)} \tag{2.2}$$

by a constant, under the agreement that $\alpha \ll W \ll \beta$ or $\beta \ll W \ll \alpha$. Their argument is verified in [10] if W is bounded for any $t > 0$. However, there is a case that $W = e^{\Psi}$ is unbounded, where this simplification is not valid.

Nevertheless, the simplified case should be studied as a special case of the orignal problem. If $\alpha \ll W \ll \beta$, according to the above argument it is seen that $\Phi(W) \approx$ *a constant* $\times\, W^a$. Then (2.1) is rewritten by the following simplifed form:

$$\Psi_{tt} = D\Delta\Psi_t - aD\nabla\cdot(\Psi_t\nabla\Psi) \quad \text{in} \quad \Omega\times(0,T). \tag{2.3}$$

In this case our problem is reduced to the following:

$$
(CH)\begin{cases}
\Psi_{tt} - D\Delta\Psi_t + aD\nabla\cdot(\Psi_t\nabla\Psi) = 0 & \text{in} \quad \Omega\times(0,T) \\
\frac{\partial}{\partial\nu}\Psi|_{\partial\Omega} = 0 & \text{on } \partial\Omega\times(0,T) \\
\Psi_t(x,0) = P_0(x), \quad \Psi(x,0) = \log W_0(x) & \text{in} \quad \Omega.
\end{cases}
$$

For (CH), many results have been known. Levine and Sleeman [10] constructed the solution when $n = 1$, $D = 1$ and $a = 1, -1$. They showed the existence of a collapse solution in the case of $n = 1$ and $a = -1$ and that of blow up solution in the case of $n = 1$ and $a = 1$. On the other hand, Yang, Chen and Liu [14] proved that both time global and blow up in finite time solutions exist dependent on their choice of initial data even if $n = 1$ and $a = 1$. Further they stated that one may obtain a collapse solution to the simplified case for $a =-1$ and general spacial dimension in the same line.

In [7][9], we studied (TM) for $a < 0$ and obtained the following results. We put $\Psi(x,t) = \gamma t + u(x,t)$ in (2.1) and introduce the equation concerning $u = u(x,t)$:

$$
u_{tt} - D\Delta u_t - \nabla\cdot\left[\gamma A(t,u)e^{-\gamma t-u}\nabla u\right] - \nabla\cdot\left[A(t,u)e^{-\gamma t-u}u_t\nabla u\right] = 0 \qquad (2.4)
$$

where

$$
A = A(t,u) = \frac{aD(\alpha-\beta)e^{-\gamma t}e^{-u}}{(1+\alpha e^{-\gamma t}e^{-u})(1+\beta e^{-\gamma t}e^{-u})}.
$$

Then, we see that (2.4) is hyperbolic if $\beta > \alpha$ and $a < 0$ and henceforth we are concentrated on this case. Namely, we consider the assumption:

$$
(A)_- \quad \beta-\alpha > 0,\ a < 0 \ \left((A)_+ \quad \beta-\alpha > 0,\ a > 0\right).
$$

Instead of the boundary condition (2.2) we may impose

$$
\frac{\partial u}{\partial\nu}|_{\partial\Omega} = 0. \qquad (2.5)
$$

In terms of

$$
P_v[u] = u_{tt} - \nabla\cdot\left[\gamma A(t,v)e^{-\gamma t-v}\nabla u\right] - \nabla\cdot\left[e^{-\gamma t-v}A(t,v)u_t\nabla v\right] - D\Delta u_t, \quad (2.6)
$$

(TM) is reduced to

$$
(TM)_t\begin{cases}
P_u[u] = 0 & \text{in} \quad \Omega\times(0,\infty) \\
\frac{\partial u}{\partial\nu} = 0 & \text{on} \quad \partial\Omega\times(0,\infty) \\
u(x,0) = h_0(x), u_t(0,x) = h_1(x) & \text{in} \quad \Omega \\
\bar{u}_1 = \int_\Omega h_1 dx = 0.
\end{cases}
$$

Here, the additional assumption $\bar{u}_1 = 0$ leads to $\int_\Omega u_t dx = 0$ by the standard argument(see Kubo and Suzuki[7]).

We put $\partial_t = \partial/\partial t$,

$$\partial_x^\alpha = \left(\frac{\partial}{\partial x_1}\right)^{\alpha_1} \cdots \left(\frac{\partial}{\partial x_n}\right)^{\alpha_n}, \quad \text{and} \quad |\alpha| = \sum_{i=1}^{n} |\alpha_i|,$$

where $\alpha = (\alpha_1, \cdots, \alpha_n)$ denotes the multi-index. Now, we introduce functional spaces used in this paper. First, $H^l(\Omega)$ denotes the usual Sobolev space $W^{l,2}(\Omega)$ of order l on Ω. Next, for functions $h(t,x)$ and $k(t,x)$ defined in $\Omega\times[0,\infty)$, we put that

$$(h,k)(t) = \int_\Omega h(t,x)k(t,x)dx \text{ and } \|h\|_l^2(t) = \sum_{|\beta|\leq 1} \|\partial^\beta h(\cdot,t)\|_{L^2(\Omega)}^2(t),$$

and sometimes we write $\|h\|(t)$ for $\|h\|_0(t)$. Thus, (,) stands for the L^2 inner product on Ω.

Theorem 1.1([9;Theorem 2.1]) *Let the initial value (h_0, h_1) be sufficiently smooth, and the condition $(A)_-$ be satisfied. Then, if $\gamma > 0$ is large, we have a unique classical solution $u = u(t,x)$ to $(TM)_t$ and it holds that*

$$\lim_{t\to+\infty} \sup_\Omega |u_t| = 0. \tag{2.7}$$

From the above theorem, we get the solution (P, W) to the original problem (1.1)-(1.4) by putting $P(x,t) = \gamma + u_t(x,t)$ and $W(x,t) = e^{\gamma t + u(x,t)}$. Then, it follows that from (2.7) that

$$\lim_{t\to+\infty} \|P(\cdot,t) - \gamma\|_{L^\infty(\Omega)} = 0. \tag{2.8}$$

On the other hand, we have $P(x,0) = \gamma + h_1(x)$ and it is possible to take $h_1 = h_1(x)$ satisfying

$$\|P(\cdot,0)\|_{L^\infty} > \gamma.$$

Thus, we have the following.

Corollary 1.1([9;Corollary 2.1]). *If the same assumption as in Theorem 1.1 is satisfied, there is a collapse in* (1.1) – (1.4). *More precisely,* (2.7) *holds and consequently, it follows that*

$$\lim_{t\to+\infty} \inf_\Omega W(\cdot,t) = +\infty.$$

2.2. Uptake case for $a > 0$

Othmer-Stevens model with uptake is written as follows.

$$P_t = D\Delta P - D\nabla \cdot (\nabla \log(P/\Phi(W))) \tag{2.9}$$

$$W_t = -WP \qquad \text{in} \quad \Omega \times (0,\infty) \tag{2.10}$$

$$P\nabla(\log(P/\Phi)) \cdot \nu = 0 \qquad \text{on } \partial\Omega \times (0,T) \tag{2.11}$$

$$P(x,0) = P_0(x), \quad W(x,0) = W_0(x) \geq 0. \qquad \text{in} \quad \Omega \tag{2.12}$$

where $\Phi(W) = \left(\frac{W+\beta}{W+\alpha}\right)^a$, $a > 0$.

Putting $\Psi(x,t) = -\gamma t - u(x,t)$ for a positive constant γ, then (2.1) is reduced the following:

$$P_v[u] = u_{tt} - \nabla \cdot \left[\gamma A(t,v)e^{-\gamma t - v}\nabla u\right] - \nabla \cdot \left[e^{-\gamma t - v}A(t,v)u_t\nabla v\right] - D\Delta u_t = 0 \tag{2.13}$$

where

$$A(t,v) = \frac{aD(\beta - \alpha)}{(\alpha + e^{-\gamma t - v})(\beta + e^{-\gamma t - v})}.$$

Our problem is reduced to the following.

$$(TMU)_t \begin{cases} P_u[u] = 0 & \text{in} \quad \Omega \times (0,\infty) \\ \frac{\partial}{\partial \nu}u = 0 & \text{on} \quad \partial\Omega \times (0,\infty) \\ u(x,0) = h_0(x), u_t(0,x) = h_1(x). & \text{in} \quad \Omega \end{cases}$$

Since $P_u[u] = 0$ is a hyperbolic equation with strong dissipation in the case of $a > 0$ and $\beta > \alpha$, that is, $(A)_+$, we can find the solution to $(TMU)_t$ for sufficiently large $\gamma > 0$ in the same manner as obtained Theorem 1.1(see K-S-H[9]). Actually, if initial data $(h_0(x), h_1(x))$ are smooth enough, it is shown that the solution $u(x,t)$ is smooth and that

$$\lim_{t \to \infty} u_t(x,t) = 0. \tag{2.14}$$

Putting $P(x,t) = \gamma + u_t(x,t)$ and $W(x,t) = e^{-\gamma t - u}$, we see that $(P(x,t), W(x,t))$ satisfies (2.9)-(2.12).

Theorem 2.1. *Let the initial value (h_0, h_1) be sufficiently smooth and let the condition $(A)_+$ be satisfied. Then, if $\gamma > 0$ is large, there exists a time global smooth solution (P,W) to the problem (2.9)-(2.12) and (2.14) holds.*

Taking account of (2.14), we have the following asymptotic property of the solution.

Corollary 2.1. *Under the same assumption as in Theorem 2.1, there is a collapse in (2.9)-(2.12).*

Remark. We consider a relationship between uptake case and exponential growth case in Othmer-Stevens model in the line of the above argument. Since $W(x,t)$ is represented by $W(x,t) = e^{\gamma t+u(x,t)}$ in (1.1)-(1.4) and $W(x,t) = e^{-\gamma t-u(x,t)}$ in (2.9)-(2.12), it follows from (2.9) and (2.10) that

$$P_t = D\Delta P - D\nabla\cdot(P\nabla\log\tilde{\Phi}(\tilde{W}))$$

$$\tilde{W}_t = \tilde{W}P$$

where $\tilde{W}(x,t) = W^{-1}(x,t)$ and $\tilde{\Phi}(W) = \left(\frac{\beta W+1}{\alpha W+1}\right)^a$, $a > 0$. Especially if we consider the simplifed case $\Phi(W) = W^a$, we have $\Phi(W) = \tilde{W}^{-a}$.

3 Anderson-Chaplain model

In this section an analysis of another parabolic and ODE system modelling tumour angiogenesis is presented by Anderson and Chaplain [1], [2]. The equation describing EC(endothelial cells) migration is,

$$\frac{\partial n}{\partial t} = D\Delta n - \nabla\cdot(\chi(c)n\nabla c) - \rho_0\nabla\cdot(n\nabla f), \qquad \text{in} \qquad \Omega\times(0,\infty) \tag{3.1}$$

where $n = n(x,t)$ is the EC density, which is corresponding to $P(x,t)$ in Othmer-Stevens model, D is the cell random motility coefficient, $\chi(c)$ is the chemotactic function with respect to TAF(tumour angiogenesis factors) concentration $c = c(x,t)$, $f = f(x,t)$ is the concentration of an adhesive chemical such as fibronectin, ρ_0 is the (constant) haptotactic coefficient(see [1],[2]). It is assumed that $\chi(c)$ takes the form

$$\chi(c) = \frac{\chi_0}{1+\alpha c},$$

where χ_0 represents the maximum chemotacitic response and α is a measure of the severity of desensitisation of EC receptors to TAF. They assume that c and f satisfy the following equations respectively:

$$\frac{\partial f}{\partial t} = \beta n - \gamma_0 nf, \qquad \text{in} \qquad \Omega\times(0,\infty) \tag{3.2}$$

$$\frac{\partial c}{\partial t} = -\eta nc, \qquad \text{in} \qquad \Omega\times(0,\infty) \tag{3.3}$$

where β, γ_0 and η are positive constants. The equations are normally posed in a bounded domain Ω with no-flux boundary conditions on $\partial\Omega$. In this section we consider this model in the following form:

$$(AC)\begin{cases} \frac{\partial}{\partial t}n = D\Delta n - \nabla\cdot(\chi(c)n\nabla c) - \rho_0\nabla\cdot(n\nabla f), \\ \frac{\partial}{\partial t}f = \beta n - \gamma_0 nf, \\ \frac{\partial}{\partial t}c = -\eta nc, & \text{in} \quad \Omega\times(0,\infty) \\ \frac{\partial n}{\partial\nu}|_{\partial\Omega} = \frac{\partial c}{\partial\nu}|_{\partial\Omega} = \frac{\partial f}{\partial\nu}|_{\partial\Omega} = 0 & \text{on} \quad \partial\Omega\times(0,\infty) \\ n(x,0) = n_0(x),\ f(x,0) = f_0(x),\ c(x,0) = c_0(x), & \text{in} \quad \Omega. \end{cases}$$

Sleeman, Anderson and Chaplain [13] constructed a solution of (AC) in case c and f depends on x only in 1 or 2 dimension. A similarity between the *discrete forms* of Othmer-Stevens model and Anderson- Chaplain model was discussed in [2]. In this section we find how two models relate to each other in the continuous form. Improving the reduction process used in section 2, we reduce the system (3.1)-(3.3) to the same type of a single equation as (2.6). That is, Anderson-Chaplain model is essentially regarded as the same type of system as Othmer-Stevens model with uptake for $a > 0$ and $\beta > \alpha$ in such a sense.

According to the way used in subsection 2.2, we can show the existence of the time global smooth solution (n, f, c) of (AC), of which n collapses. In fact, by (3.2) we have

$$\frac{f_t}{(f-\beta\gamma_0^{-1})} = \frac{(f-\beta\gamma_0^{-1})_t}{(f-\beta\gamma_0^{-1})} = \frac{\partial}{\partial t}\log|f-\beta\gamma_0^{-1}| = -\gamma_0 n$$

and (3.3) gives

$$\frac{c_t}{c} = \frac{\partial}{\partial t}\log c = -\eta n.$$

In subsection 2.2 the procedure from (2.1) to $(TMU)_t$ is the key process to obtain the solution of (2.9)-(2.12). Recalling that (2.1) is reduced from the exponential growth case, instead of (3.1)-(3.3) we should consider the problem (3.1) and

$$\frac{\partial}{\partial t}\log|f-\beta\gamma_0^{-1}| = \gamma_0 n \quad \text{and} \quad \frac{\partial}{\partial t}\log c = \eta n. \tag{3.4}$$

Put $\log c(x,t) = \Psi(x,t)$ and $n(x,t) = \eta^{-1}\Psi_t(x,t)$, then we set

$$f(x,t) = \beta\gamma_0^{-1} + e^{\eta^{-1}\gamma_0\Psi(x,t)}(f_0(x) - \beta\gamma_0^{-1})c_0(x)^{-\eta^{-1}\gamma_0}.$$

In terms of $\psi(x) = c_0(x)^{-\eta^{-1}\gamma_0}(f_0(x)-\beta\gamma_0^{-1})$, (3.1) and (3.4) are reduced to

$$\Psi_{tt} = D\Delta\Psi_t - \nabla\cdot\left(\frac{\chi_0 e^{\Psi}}{1+\alpha e^{\Psi}}\Psi_t\nabla\Psi\right) - \nabla\cdot(\rho_0\eta^{-1}\gamma_0\Psi_t e^{\eta^{-1}\gamma_0\Psi}\psi(x)\nabla\Psi)$$
$$-\nabla\cdot(\rho_0\Psi_t e^{\eta^{-1}\gamma_0\Psi}\nabla\psi(x)). \tag{3.5}$$

If $\psi(x) > 0$, (3.5) is regarded as the same type of equation as (2.1) under the condition $(A)_+$. Hence by the same way as in the proof of Theorem 2.1 we obtain the energy inequality and show the existence of the solution.

Theorem 3.1. *Let the initial value* $(n_0(x), f_0(x), c_0(x))$ *be sufficiently smooth and let* $\psi(x) > 0$. *There is a classical solution* $(n(x,t), f(x,t), c(x,t))$ *of* (AC) *such that it holds*

$$\lim_{t\to+\infty} \|n(x,t) - \bar{n}_0\|_{L^\infty(\Omega)} = 0, \tag{3.6}$$

$$\lim_{t\to+\infty} \|c(x,t)\|_{L^\infty(\Omega)} = 0, \tag{3.7}$$

$$\lim_{t\to+\infty} \|f(x,t) - \frac{\beta}{\gamma_0}\|_{L^\infty(\Omega)} = 0, \tag{3.8}$$

where $\bar{n}_0$ *stands for the spatial average of* $n_0(x)$.

The sketch of the proof of Theorem 3.1. Putting $\Psi = -\gamma t - u$ in (3.5), (AC) is reduced to the same type of problem of $u(x,t)$ as $(TMU)_t$. By deriving the energy estimate of it, it is shown that (n, f, c) is the solution to (AC). Then (3.6)-(3.8) follows from the fact that $\lim_{t\to\infty} u(x,t) = 0$. The more details of the proof is shown in Kubo-Suzuki-Hoshino[9].

Since $n(x,t)$ is corresponding to $P(x,t)$ in Corollary 1.1, the same argument gives the following.

Corollary 3.1. *Under the same assumption as in Theorem 3.1, there is a collapse in* (AC).

Finally in this section, we give a comment on existence of a Lyapunov function for the system (AC). Here, we assume

$$\gamma_0 f_0(x) > \beta. \tag{3.9}$$

It follows from (AC) that $\gamma_0 f(x,t) > \beta$ for $x \in \Omega$, $t > 0$. If we define

$$g(x,t) = \frac{\gamma_0}{\beta} f(x,t) - 1 \tag{3.10}$$

for $x \in \Omega$, $t > 0$, then we have $g(x,t) > 0$ and $g_t = -\gamma_0 n g$.

We obtain the following result (cf. [9, Appendix]).

Theorem 3.2. *Suppose that* (3.9) *holds. Let* $L(t)$ *be*

$$L(t) = \int_\Omega \left[n(\log n - 1) + \frac{\chi_0}{2\alpha^2\eta} \frac{1+\alpha c}{c} |\nabla \log(1+\alpha c)|^2 + \frac{\beta\rho_0}{2\gamma_0^2} g |\nabla \log g|^2 \right] dx,$$

where g is defined by (3.10). *Then, $L(t)$ is a Lyapunov function for* (AC).

Indeed, we can show

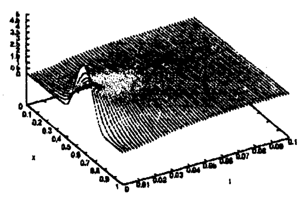
$$\frac{d}{dt}L(t) = -D\int_\Omega p^{-1}|\nabla p|^2dx - \frac{\chi_0}{2\alpha^2}\int_\Omega \frac{p}{c}|\nabla \log(1+\alpha c)|^2dx - \frac{\beta\rho_0}{2\gamma_0}\int_\Omega pg|\nabla \log g|^2dx.$$

4 Numerical experiments

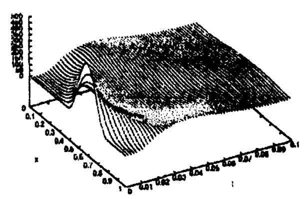
In this section, we report some results of numerical experiments for Othmer-Stevens model with a linear growth in $S^1 = \mathbf{R}/\mathbf{Z}$;

$$(OSL)\begin{cases} P_t = (P_x - aPW_x)_x & (x \in S^1,\ 0 < t < T), \\ W_t = P & (x \in S^1,\ 0 < t < T), \\ P(x,0) = P_0(x) \geq 0, \not\equiv 0, & (x \in S^1) \\ W(x,0) = W_0(x). & (x \in S^1). \end{cases}$$

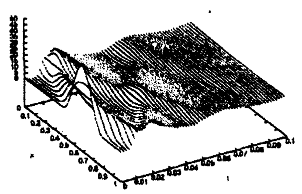
In Fig 1, we plot numerical solutions to $P(x,t)$ for $a = -1, -50$, and $\lambda = \|P_0\|_{L^1(S^1)} = 1, 100$ and $W_0(x) \equiv 0$. We can observe that there are decaying traveling waves when the effect of chemotaxis is stronger than that of diffusion.



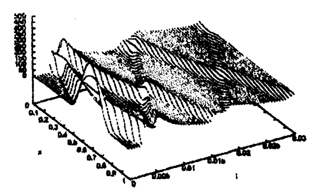
(i) $a = -1.0$, $\lambda = 1.0$, $T = 0.1$



(ii) $a = -1.0$, $\lambda = 100.0$, $T = 0.1$



(iii) $a = -50.0$, $\lambda = 10.0$, $T = 0.1$



(iv) $a = -50.0$, $\lambda = 100.0$, $T = 0.03$

Figure 1: Behavior of numerical solutions for $P(x,t)$ with $\lambda = \|P_0\|_{L^1(S^1)}$.

Let us briefly describe our finite difference approximation, which is based on the conservative upwind finite difference approximation proposed by [12].

Take a positive integer N and let $h = 1/N$. We introduce two kinds of mesh points over S^1 as

$$x_j = \left(j - \frac{1}{2}\right) h \quad \text{(main mesh)}, \qquad \hat{x}_j = jh \quad \text{(dual mesh)}.$$

We find approximations of P and W over the main mesh points and dual mesh points, respectively;

$$P_j^n \approx P(x_j, t_n) \quad \text{and} \quad W_j^n \approx W(\hat{x}_j, t_n),$$

where t_n is a discrete time step defined as $t_n = \tau_1 + \cdots + \tau_n$ and τ_j's are determined by the algorithm described below. The initial condition is approximated by

$$P_j^0 = P_0(x_j), \qquad W_j^0 = W(\hat{x}_j). \tag{4.1}$$

Suppose that $\{P_j^{n-1}\}_{j=1}^N$ and $\{W_j^{n-1}\}_{j=0}^{N+1}$ have been obtained for $n \geq 1$. Then we approximate $aW_x(\cdot, t_{n-1})$ by $b_j^{n-1} = a(W_j^{n-1} - W_{j-1}^{n-1})/h$ and set $b_j^{n-1,\pm} = \max\{0, \pm b_j^{n-1}\}$. Following a technique of upwind approximation, we may suppose that P_j^n and P_{j+1}^n are carried into a point $\hat{x}_j$ on flows $b_j^{n-1,+}$ and $-b_{j+1}^{n-1,-}$, respectively. That is, the approximation F_j^n of the flux $P_x - aPW_x$ at $(\hat{x}_j, t_n)$ is calculated by

$$F_j^n = \frac{P_{j+1}^n - P_j^n}{h} - b_j^{n-1,+} P_j^n + b_{j+1}^{n-1,-} P_{j+1}^n.$$

Based on the observation above, our present scheme is as follows

$$\frac{P_j^n - P_j^{n-1}}{\tau_n} = \frac{F_j^n - F_{j-1}^n}{h}, \qquad \frac{W_j^n - W_j^{n-1}}{\tau_n} = P_j^{n-1}. \tag{4.2}$$

Time increment τ_n is chosen as

$$\tau_n = \min\left\{\tau, \ \frac{\varepsilon}{2\max_j |b_j^{n-1}|}\right\}, \tag{4.3}$$

where $\tau > 0$ and $\varepsilon \in (0, 1)$ are constants. Then we can show that

$$P_j^n > 0 \quad (\forall j, \forall n \geq 1), \qquad \sum_{j=1}^N P_j^n h = \sum_{j=1}^N P_j^0 h \tag{4.4}$$

in the same manner as that of [12]. We note that (4.4) is a discrete version of analytical properties of a solution to (OSL).

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